VOL. 10, No. 1 JANUARY 1956

CHRONICLE OF THE WORLD HEALTH ORGANIZATION

CONTENTS

	Page
Poliomyelitis vaccination: a preliminary review	3
Occupational health	14
Mortality from ulcers of the stomach and duodenum	20
Notes and News	
WHO-sponsored visit of medical scientists to Egypt	23
Malaria-control programme planned for Sudan	23
Trachoma survey in Jordan	23
Training of auxiliary health personnel in Libya	23
Meeting of fellowship administrators	23
Heart operations	24
Seminar on the teaching of preventive medicine	24
Review of WHO Publications	25
International Non-Proprietary Names for Pharmaceutical Preparations	26

SCHEDULE OF MEETINGS

1956

9 January	**Standing Committee on Administration and Finance, Geneva**
17 January	**Executive Board, seventeenth session, Geneva**

The mention of manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature which are not mentioned. Proprietary names of such products are distinguished by initial capital letters.

PRINTED IN SWITZERLAND

POLIOMYELITIS VACCINATION

A Preliminary Review

Since 1954, field trials of poliomyelitis vaccination have been carried out in several countries, particularly in the USA. Accidents in the use of the vaccine in the USA have been the source of considerable doubt on the part of public health authorities in a number of countries, and vaccination programmes which began most auspiciously have been stopped.

In late November 1955, the World Health Organization convened in Stockholm a group of experts [1] *qualified to review the present position with regard to poliomyelitis vaccination and to provide some measure of guidance for public health authorities. In the article which follows, the introduction and the sections on experience with poliomyelitis vaccination in various countries and on public health application of the vaccine are extracts from the report of this group. An indication of the contents of the more technical parts of the report is given in the paragraph on problems relative to vaccine production and administration, and the article concludes with a summary of the group's general recommendations. The full report will be published in the* Technical Report Series *early in 1956.*

The discovery by Enders, Weller, and Robbins that poliovirus would multiply in tissue cultures of non-nervous human cells has had many applications. Already it has fulfilled much of its early promise, and important advances in knowledge of poliomyelitis have been made.

It was apparent that this technique could be applied to the production of large amounts of poliovirus, which could, in turn, be used for the preparation of vaccine. The task of developing this vaccine was undertaken by Dr J. E. Salk, aided by the National Foundation for Infantile Paralysis of the United States. He and his associates, in a long series of studies, worked out methods of producing suspensions of poliovirus suitable for the preparation of an inactivated vaccine. They defined conditions for inactivation of the virus suspensions with formaldehyde and described in detail the control of the process of inactivation. They also described a neutralization test of value in determining the antibody response in inoculated human beings and experimental animals.

Based on the principles and methods prescribed by Salk, a formalin-treated poliomyelitis vaccine has been produced in large quantities in the USA and in several other countries.

A large-scale field trial of this vaccine was carried out in the USA in 1954 under carefully controlled conditions. The results of this trial [2] were carefully and thoroughly evaluated by a team under Dr T. Francis, and the results of the study were announced in early April 1955. In brief, the findings were that the vaccine was safe and effective.

[1] Members of the group were: Dr Karl Evang, Director-General of Public Health, Oslo, Norway (*Chairman*); Dr S. Gard, Professor of Virus Research, School of Medicine, Karolinska Institutet, Stockholm, Sweden (*Vice-Chairman*); Dr J. H. S. Gear, Director of Research, Poliomyelitis Research Foundation, South African Institute for Medical Research, Johannesburg, Union of South Africa (*Rapporteur*); Professor R. Haas, University of Freiburg, Freiburg, Germany; Dr A. D. Langmuir, Communicable Disease Center (Public Health Service), Department of Health, Education, and Welfare, Atlanta, Ga., USA; Professor P. Lépine, Chef du Service des Virus, Institut Pasteur, Paris, France; Dr H. von Magnus, Statens Seruminstitut, Copenhagen, Denmark; Dr F. P. Nagler, Department of National Health and Welfare, Ottawa, Canada; Dr J. R. Paul, Professor of Preventive Medicine, Yale University School of Medicine, New Haven, Conn., USA; Dr W. L. M. Perry, Director, Department of Biological Standards, National Institute for Medical Research, London, England; Dr A. B. Sabin, Professor of Research Pediatrics, University of Cincinnati College of Medicine, The Children's Hospital Research Foundation, Cincinnati, Ohio, USA; and Professor E. T. C. Spooner, London School of Hygiene and Tropical Medicine, London, England. The Secretariat was represented by Dr W. M. Bonne, Director, Division of Communicable Disease Services, WHO; Dr J. T. Warren, Science Attaché, American Embassy, Stockholm, Sweden (Consultant, WHO); and Dr A. M.-M. Payne, Chief, Section of Endemo-epidemic Diseases, Division of Communicable Disease Services, WHO (*Secretary*).

[2] Vaccine Evaluation Center, University of Michigan (1955) *Evaluation of 1954 field trial of poliomyelitis vaccine*, Ann Arbor

Immediate steps were taken to apply the vaccine in the USA on a very large scale, and preparations were also made in a number of other countries. Probably never in the history of medicine had a new public health measure been applied on a mass scale so rapidly after the painstaking laboratory research which led to its development. It was almost inevitable, therefore, that this transition should be attended by serious difficulties.

In many countries of the world, information concerning the vaccine reached the public through the popular press before detailed scientific information had reached the scientists. The enthusiasm with which the news was received was a natural reflection of the great importance of the discovery and of the fear of poliomyelitis which exists in so many countries. Many health authorities were therefore at once subjected to heavy pressure of public opinion to apply the new control measure at the earliest possible moment.

News of accidents following use of the vaccine in the USA led to considerable confusion, both among the general public and among health authorities who were not fully aware of the many problems still remaining to be solved. This confusion has, to a large extent, persisted in many parts of the world, and many health authorities are finding it difficult to decide whether or not they should take steps to bring the new control measure into general use and, if so, what these steps should be.

However, during the late spring, summer, and autumn of 1955, the vaccine was used on a large scale in the USA, Canada, and Denmark, and on a smaller scale in Germany and South Africa. The time is opportune to review the experiences in the use of this vaccine in each of these countries in turn, as well as those of France and Sweden where the problems of vaccination have also been under investigation.

Experience with poliomyelitis vaccination in various countries

The best assessment of the safety and efficacy of any vaccine intended for human use is the result of its use in man. The experts at the WHO meeting therefore summarized the experience of the use of poliomyelitis vaccination in man in their respective countries, with brief details of the composition and method of preparation of the vaccine used. It was emphasized, however, that much of the information was preliminary in nature and necessarily incomplete, and in no way purported to be a full report of national experience.

The group noted a preliminary report [3] of the field experiences with poliomyelitis vaccine in the USA in 1955. Two main problems were considered: the safety of the vaccine, and the evaluation of the effectiveness of the rather extensive vaccinations that were performed. Dr A. D. Langmuir provided a summary of parts of this report.

Both epidemiological and laboratory evidence established that certain lots of vaccine, distributed by one laboratory, contained poliomyelitis virus in infective amounts. A total of 204 vaccine-associated cases occurred. Of these, 79 were among vaccinated children, 105 among family contacts of vaccinated children, and 20 among community contacts. Approximately three-fourths of the cases were paralytic. There were 11 deaths, making a case fatality rate of 5%.

The onset of the cases among vaccinated children was concentrated in the interval from 4 to 14 days following inoculation, whereas the onset of the family contact cases was concentrated in the period from 15 to 28 days, which represents a double incubation period. The small number of community contact cases occurred at intervals somewhat

[3] Langmuir, A. D., Nathanson, N. & Hall, W. J. (1956) The surveillance of poliomyelitis in the United States in 1955 (to be published in the *American Journal of Public Health* in January 1956)

longer than those of the family contact cases. First paralysis began in the inoculated extremity in two-thirds of the paralytic cases among vaccinated children. This relationship is very similar to that reported by Bodian for cynomolgus monkeys injected intramuscularly with Mahoney virus.

Isolation of poliovirus was reported in association with about half of the paralytic cases and one-third of the non-paralytic cases. Type 1 virus was identified in all but two of these instances, and types 2 and 3 were found only once.

Laboratory tests performed on the 17 lots of vaccine distributed by the laboratory in question resulted in isolation of poliovirus from seven lots. Type 1 virus was isolated from six of these lots; type 2 virus was also found in one of these lots, and type 3 virus in two of them. In the seventh positive lot types 2 and 3 virus were found. Attack rates of associated cases by individual lots of vaccine revealed the highest rates for the six lots from which type 1 virus was isolated.

A small number of cases of poliomyelitis was also associated with a single lot of vaccine distributed by another laboratory. The epidemiological relationships of these cases raised strong suspicion of some explanation other than coincidence. However, extensive laboratory tests of this lot have failed to demonstrate poliovirus.

During the period from 12 April to 7 May, approximately 4 million doses of poliomyelitis vaccine manufactured by five different laboratories were administered to children in the USA. Except for the cases associated with several lots of vaccine from one laboratory and the single lot of vaccine from another no other situation involving the possibility of unsafe lots of vaccine was recognized.

Late in May new safety standards were promulgated. Up to 15 November approximately 21 million additional doses had been released throughout the country for general use by both health departments and private physicians. The actual number of children inoculated is not yet known. A constant nation-wide surveillance for the occurrence of vaccine-associated cases has been maintained, and no incident has come to light that tends to incriminate any lot of vaccine, from any manufacturer, that has been used since May 1955.

The limitation of vaccine supplies resulted in the restriction of inoculations to first and second grade schoolchildren. The great majority of these received only a single injection before mid-September, when schools reopened following summer vacation. Thus a unique opportunity for evaluation studies was presented. Many States rapidly developed plans for special studies, in collaboration with the Communicable Disease Center of the Public Health Service.

Preliminary reports up to 1 November were received from 11 States and one city. They revealed attack rates for paralytic cases from two to more than five times greater among unvaccinated children than among vaccinated children in the same age groups. Attack rates for non-paralytic cases showed less marked but generally favourable reductions.

In evaluating these preliminary reports many possible sources of error must be kept in mind, and substantial changes from the preliminary findings can be expected when final reports are completed. However, the consistency of the favourable differences in paralytic rates in all areas is most encouraging.

An independent method of evaluating the effectiveness of the vaccine was found in an analysis of age-specific attack rates by individual years of age. Since vaccinations were restricted largely to first and second grade schoolchildren, a discontinuity in the rates for 7- and 8-year-old children could be anticipated if the vaccines were effective. Preliminary analyses of data submitted from

33 States for the period from 3 July to 14 October revealed that the attack rates for paralytic cases among the 7- and 8-year olds were definitely lower than the rates for either younger or older children or adolescents. Thus independent evidence was found indicating the effectiveness of the vaccine as used in the USA in 1955. Also encouraging was the fact that this beneficial effect followed in large degree the administration of a single dose of vaccine.

Dr F. P. Nagler reported that in Canada production of the poliomyelitis vaccine was undertaken by the Connaught Laboratories, Toronto, using the Maitland tissue-culture technique. Rhesus monkey kidney tissues were employed. Formalinization after sintered-glass filtration, and neutralization of the formalinized monovalent strain pools were carried out in a fashion similar to that recorded in the Minimum Requirements of the National Institutes of Health (NIH), Bethesda, Md., USA.[4] The strains of virus employed were the same as those used in vaccines prepared by the American manufacturers. Monovalent and trivalent vaccines were tested in tissue cultures and monkeys by the Connaught Laboratories according to the Minimum Requirements of the NIH. Twenty-five lots of trivalent vaccine were submitted to the Department of National Health and Welfare, Ottawa, for clearance under the Canadian Food and Drug Act. The Department tested each of these lots in monkeys and tissue cultures, along the lines of the NIH Minimum Requirements, with the exception that each tissue-culture passage was observed for one week more than is specified by the USA requirements.

The Connaught vaccine was purchased by the Department of National Health and Welfare and the provincial departments of health, which shared the costs equally. It was distributed by the provincial departments of health to their regional medical officers, who organized and supervised the vaccination programme.

Approximately 860 000 children between the ages of 6 and 9 years received injections during the months of April to June 1955. In most of the provinces two doses of vaccine, spaced four weeks apart, were given. Two provinces administered three doses. The great majority of children received the injection of the vaccine subcutaneously, while approximately 100 000 children were given the vaccine intramuscularly.

A surveillance team was established in each province and investigated each case of poliomyelitis, both in vaccinated children and in unvaccinated children of the same age groups. Three cases of paralytic poliomyelitis were reported in children within four weeks after vaccination. A thorough investigation of these cases showed that there was only one case in which there might possibly have been a relationship between the vaccination and the disease. Preliminary and incomplete results from some provinces up to the end of October show a significant reduction in the incidence of paralysis in the vaccinated children compared with unvaccinated children of similar age groups.

Production of the vaccine at the Connaught Laboratories has again been resumed, employing methods of filtration and control similar to those described in the amended NIH Minimum Requirements. Primary vaccination of first and second grade schoolchildren will be resumed early in 1956; and, at the same time, a booster dose will be given to the children who received their first two injections during the spring of 1955.

Experience in Denmark was summarized by Dr H. von Magnus. In Denmark epidemics of poliomyelitis have presented a serious problem for many years; but the epidemic in the fall of 1952, with a total of 2450 paralytic cases in a population of about

[4] United States Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health (1955) *Minimum requirements: poliomyelitis vaccine*, Bethesda

4.5 million (a rate of 56.5 per 100 000 population), was the most severe in the history of the country, the range during the previous ten years having been from 0.5, in 1951, to 25.5, in 1944. Therefore, as soon as the results of the large field trial in the USA in 1954 were available, it was decided to start poliomyelitis vaccination immediately. Accordingly, a vaccine prepared at Statens Seruminstitut, closely following the methods described by Salk and his co-workers, was made available for all children in the first five grades in school (approximately 7-12 years of age). The vaccination programme started on 25 April 1955, and it resulted in the vaccination, during April, May, and June, of approximately 425 000 children, representing about 98% of the children in these age groups.

Tissue cultures prepared from trypsinized monkey kidney tissue cells were used for growing poliovirus. The virus strains selected to represent poliovirus types 1, 2, and 3 were respectively the Brunhilde, MEF1, and Saukett strains. The MEF1 and Saukett strains were received from Dr Salk's laboratory, and are the same as those used by the manufacturers of poliomyelitis vaccine in the USA. The tissue-culture passage of the Brunhilde strain originated from Dr J. F. Enders' laboratory, and had undergone 12 passages in human tissue culture and, subsequently, about 6 passages in monkey kidney tissue.

Safety tests similar to those outlined in the NIH Minimum Requirements of 26 May had been carried out on the vaccine before its release for use.

The vaccine inoculations were given intradermally in two simultaneous injections of 0.1-0.15 ml each, a total of 0.2-0.3 ml per dose. This procedure was repeated after 4-6 weeks, and a third dose will be given 9-12 months after the first. The reactions following the administration of the vaccine by the dermal route were mild and infrequent, consisting mainly of local swelling of the arm on the site of inoculation. A preliminary estimate indicated that this occurred in 0.1%-0.2% of the children.

No cases of paralysis occurred in any of the vaccinated children in association with the vaccination, and no other serious reactions were observed in the children.

Blood samples were obtained before vaccination from approximately 2300 children in the second grade of school. A preliminary screening of 2100 of these prevaccination serum samples was carried out. It was found that 13% of these 8-year-old children had no antibodies to any of the three types of poliovirus. Antibodies to all three types were found in 24% of the sera.

A preliminary study on the antibody response to vaccination in 48 of these children indicated that, while the type 2 and type 3 strains seemed to have a satisfactory antigenicity under the given circumstances, it would be of advantage if a more antigenic type 1 strain could be incorporated in the vaccine in the future.

From 1 July to November 1955 a total of approximately 250 000 children in the age groups 9 months to 7 years had had one or two inoculations of vaccine. No serious reactions were observed in these children.

The protective effect of the polio vaccination carried out in Denmark so far cannot be evaluated, since the incidence of poliomyelitis was extremely low in 1955; only seven clinical cases of paralytic poliomyelitis had been reported up to November.

Information on studies in France was supplied by Professor P. Lépine. Since 1951, the Virus Division of the Institut Pasteur, Paris, has been selecting and studying poliovirus strains of the different types with a view to their application to vaccination. The production of an inactivated vaccine was considered mainly as an interim measure pending consideration of the use of a live attenuated vaccine in the future. Before any

attempt at mass production of a vaccine was made, preliminary studies were carried out for over one year on the modification of synthetic media derived from Connaught No. 199 medium to the culture requirements of susceptible cells, such as renal epithelial cells from different African monkey species, or fibroblasts of human origin. Since the completion of a specially equipped laboratory for vaccine production, studies have been carried out on the virus yield of cultures under different conditions; on the influence of storage, filtration, temperature, and methods of inactivation on the quality of the final product; and on antigenicity and innocuity tests. Production has gradually been raised to a level of 100 litres per week and some vaccine stockpiled for future use, should the health authorities decide on a vaccination programme.

A group of children, 2 to 7 years of age with no poliovirus antibody, were vaccinated by three subcutaneous injections of an inactivated vaccine, and the antibody level had been carefully observed over a period of 14 months up to the date of the WHO meeting. At the same time a serological survey of the juvenile population was carried out. This survey is being extended to the different age groups and socio-economic levels of the population.

No attempts have been made at mass vaccination in France. A programme for an extended trial vaccination was planned but was withheld pending further information when news of accidents following the use of vaccine in the USA was received.

Professor R. Haas reported that in Germany the production of poliomyelitis vaccine on a large scale has been in progress in the Behringwerke since 1954. So far more than 1500 litres of inactivated virus fluids have been produced.

The virus was grown on trypsinized rhesus or cynomolgus kidney cells, using Connaught No. 199 medium diluted with Hank's solution. The strains used were the Mahoney strain for type 1, MEF1 for type 2, and Saukett for type 3. In September 1955 the Brunhilde strain was substituted for the Mahoney strain. Seitz filtration was used in the production process. Inactivation was performed with formaldehyde. During the first months the vaccine produced was controlled by four different laboratories according to the methods described in the NIH Minimum Requirements and its various amendments, with the exception that larger samples were tested. In March 1955 the Paul Ehrlich Institute, Frankfurt-on-Main, took over the control of the vaccine o behalf of the Government. Control was carried out according to regulations prescribed by the Government of the State of Hessen.

Vaccinations started in November 1954 and were continued until the last week of May 1955. The vaccinations were then stopped, following paralysis of two monkeys out of three after intracerebral injection of a special sample of the vaccine. Retests by the Paul Ehrlich Institute on a large scale were entirely negative. But, since, in the meantime, news of the accidents in the USA had been received, the vaccinations were not recommended; and new regulations were formulated in accordance with the Technical Report on Salk Poliomyelitis Vaccine (June 1955).[5] It was expected that the new regulations would be put into force at the end of 1955, and that vaccinations would then be recommenced.

From November 1954 till May 1955 nearly 100 000 vaccinations were performed. The exact figures are not known, because many vaccinations were carried out by general practitioners. About 10 000 individuals were vaccinated by paediatric clinics of different universities and by the medical service of

[5] United States Department of Health, Education, and Welfare, Public Health Service (1955) *Technical report on Salk poliomyelitis vaccine*, Washington, D.C.

the Behringwerke and affiliated plants. Questionnaires sent in by the doctors showed that no serious reactions had occurred.

It is believed that most vaccinations were performed on children in the age groups from 1 to 10 years and 10 to 15 years, but a certain number of older individuals were also vaccinated including some doctors, nurses, and parents. Only a few children received the full course of three injections; most received two, and an unknown number only one. In most cases the vaccine was administered subcutaneously or intramuscularly. At the time of the WHO meeting, no case of paralytic poliomyelitis in a vaccinated child had been reported. In one instance a vaccinated child was thought to have died from poliomyelitis, but this could not be confirmed by laboratory tests. Samples of blood were taken from several hundred of the vaccinated children; tests are still under way, and the results are not yet available.

Dr J. H. S. Gear reviewed the position of poliomyelitis vaccination in South Africa. Vaccine has been produced on a large scale in the laboratories of the Poliomyelitis Research Foundation since 1954. With minor modifications in the process of formalinization, the methods of production have been similar to those worked out in the USA. Trypsinized kidney cells derived from the common South African vervet monkey *Cercopithecus aethiops pygerythous* have been used for the preparation of the tissue cultures for the growth of poliovirus.

The strains of virus used were: type 1—Brunhilde strain; type 2—Collans strain, isolated by Professor van den Ende in Cape Town from the central nervous system of a fatal adult case; and type 3—Templeon strain, isolated by Dr N. H. Malhuhe from the faeces of a child with a silent infection who had been in contact in a nursery school with another infant who died of bulbar poliomyelitis. The Collans and Templeon strains were chosen originally because they regularly produced high titres of virus in tissue culture and were local South African strains.

The vaccine which has been issued in South Africa was prepared from these strains, but recently it was decided to substitute relatively non-virulent strains for them. These are, at present, undergoing further virulence and antigenicity tests.

Approximately 1000 litres of virus suspension have been produced, but only 200 litres have been processed to prepare vaccine.

A committee consisting of virus and public health experts was appointed to advise the Minister of Health on the issue of this vaccine. When the first reports of cases of paralytic poliomyelitis associated with vaccination in the USA were received, it was decided that the issue of vaccine be delayed, and the committee recommended that all the vaccine which had passed the NIH Minimum Requirements then in force shoud be retested according to the requirements of the United States Public Health Service as of 26 May 1955. This was done, and the results were negative.

Vaccine sufficient to inoculate 16 000 children was released in September 1955. A priorities committee considered applications for this vaccine and decided that children under 6 years old and children up to 16 years old of doctors, nurses, and others whose occupation brought them into unusually close contact with infections should be given first priority.

No case of paralytic poliomyelitis has been reported among the more than 15 000 children receiving the vaccine. Two cases of illness suspected of having been non-paralytic poliomyelitis were investigated and found to be due to other infections. Two mild skin rashes, probably of allergic origin, were also reported.

Blood specimens have been collected for antibody studies from a representative sample of those vaccinated, but these studies are

not complete, and the results are not yet available.

Professor S. Gard reported that in Sweden a formalin-treated poliovirus vaccine has been produced and tested on a small scale. The virus was grown in human embryonic tissue culture and inactivated with formaldehyde of 0.006 molarity for 11 days at 25°C.

In February and March 1955 a field trial on about 2000 schoolchildren in Stockholm was carried out. The experiment was designed as an antigenicity test to permit a direct comparison with the results obtained in the laboratory. Furthermore, the subcutaneous and intradermal routes of inoculation were compared and also the effect of intervals of three and six weeks between the first and second inoculations.

No serious side reactions of any kind were observed. Neutralization tests were carried out on pre- and post-inoculation sera. Although the numbers of children in each test group were too small to permit definite conclusions, the results appeared encouraging....

A vaccination campaign had been planned for the spring of 1955 pending the publication of the report on the field trial in the USA in 1954. However, after the release of the news of accidents following vaccination in the USA, and on account of the failure of some batches of Swedish vaccine to pass the safety tests, the vaccination programme was called off.

* * *

The foregoing information on the experience in their respective countries presented by the members of the WHO expert group provided evidence that poliomyelitis vaccine had been successfully used on a relatively large scale in a number of countries. In the USA certain batches of vaccine were responsible for causing paralytic poliomyelitis in a small proportion of the children inoculated with them. In other instances, their use resulted in the introduction of infection into a household, where it became manifest by the occurrence of a paralytic case in an uninoculated sibling or parent. In a few instances, there was a further limited spread in the community in which the family or child lived.

Except for these incidents associated with a few lots of vaccine, in which the total cases numbered about 200, several million children were inoculated without mishap in the USA. It has recently become clear that this was of considerable benefit in reducing the incidence of paralytic poliomyelitis, the rate being significantly lower among the vaccinated children as compared with the unvaccinated children of similar age groups.

The preliminary reports available for Canada have also shown a significant reduction in the incidence of paralysis in the vaccinated children, as compared with unvaccinated children of similar age groups. This age group, as in the USA, is predominantly 7 to 9 years, which is the only age group in which the effectiveness of the vaccine has so far been demonstrated. Sufficient information is not available at present to draw conclusions for other age groups.

In Denmark, Germany, and South Africa, poliomyelitis vaccine has been produced on a relatively large scale; and approximately 800 000 children have been safely inoculated, with no serious untoward reactions. It is still too early to assess the value of the vaccine in these countries in preventing paralytic poliomyelitis.

Only time will tell how long the benefit conferred by vaccination will last. A full appraisal of its value will not be possible until children inoculated in early childhood have grown up and passed through the years of childhood and adolescence, when they are most liable to suffer from paralytic poliomyelitis.

Although it has been clearly demonstrated that a safe and effective formalin-treated

vaccine can be produced, it is equally evident that its production is associated with some uncertainty and presents problems which merit consideration.

Problems relative to vaccine production and administration

The group of experts discussed in detail several aspects of the preparation of vaccine and of vaccination: safety testing of vaccines, including control of the inactivation process, the final tissue-culture safety test, the monkey safety test, and other safety tests; selection of strains for inactivated poliomyelitis vaccine; antigenicity tests; theoretical complications of vaccination against poliomyelitis; live virus vaccines; and design and techniques of serological surveys. It also outlined the most important problems on which further research is needed, with emphasis on those contributing to ensuring the safety of the vaccine.

Public health application of inactivated poliomyelitis vaccine under different epidemiological conditions

The main concern of the WHO group was to try to determine, on the basis of the information available on experience to date, to what extent poliomyelitis vaccination at its present stage of development should be applied on a large scale. The group accordingly weighed the considerations facing public health authorities and tried to establish some guiding principles for reaching a decision on whether or not to vaccinate against poliomyelitis.

There are a number of questions to which the health officer needs an answer before he can decide whether or not to recommend poliomyelitis vaccination as a general public health measure.

The first question is whether the vaccine is safe for use on a mass scale, and whether commercial production is sufficiently developed to produce a safe product consistently. . . . It should be noted that, apart from the major incident described on page 4 and one relatively minor incident not as yet fully clarified, there has been no evidence that the vaccine caused poliomyelitis among the 10 million or more children who have been inoculated. The latest developments in production techniques and methods of testing should be a further assurance of the safety of the product.

The second question is whether the vaccine is effective. The conclusions of the report on the field trial in the USA in 1954,[6] and the experience outlined on pages 4 to 10, show that it has been proved to be effective under certain conditions in schoolchildren between the ages of 6 and 10. Adequate information is still lacking as to its effectiveness in other age groups, and information is especially needed regarding very young children. Nor is it known how effective it will be under very different epidemiological circumstances.

The third question health authorities may ask is whether the vaccine should be applied on a mass scale everywhere, or whether its use should be restricted to specific epidemiological conditions, and whether there are circumstances in which it is inadvisable to apply mass vaccination. The answer should be derived from two main considerations, which are to some extent interdependent. On the one hand, there is the seriousness of the problem of poliomyelitis in the country concerned, that is to say, the incidence of paralytic disease. The age incidence must also be considered, since paralytic poliomyelitis tends to be more severe in adult life. On the other hand, there are the cost and the practicability of a mass vaccination programme, which must be considered in relation to the funds and facilities available, to the other demands upon the available funds,

[6] Vaccine Evaluation Center, University of Michigan (1955) *Evaluation of 1954 field trial of poliomyelitis vaccine*, Ann Arbor

and to the saving in human suffering and in the cost of hospital and social care.

In many countries it may be difficult to determine these facts. Reliable statistical information may be lacking. Every effort should therefore be made to determine the actual situation in the country before reaching a decision. This information will also be essential for the planning of a mass programme. If such a programme is planned, a decision will have to be made as to which age groups to immunize. There are two ways in which this could be done. The first is by a study of the age incidence of paralytic poliomyelitis, preferably accumulated over a number of years. For example, it has been confirmed by serological studies that, where environmental sanitation is still inadequate, the disease is usually predominantly infantile, 90% or more of the cases occurring in the first two or three years of life, and that almost everyone over the age of 5 is immune. Thus there is no point in vaccinating those over 5 years old. On the other hand, in countries where as many as one-third of all cases occur over the age of 15, it may be necessary to vaccinate persons up to the age of 40 or even older.

In many areas reliable information regarding the age incidence of poliomyelitis is lacking. Where this is so, every effort should be made to improve the collection of morbidity statistics as soon as possible. As an interim measure, valuable information can be obtained from properly designed serological surveys to determine the immunity status of the population.... It should be emphasized, however, that, where adequate morbidity statistics are available, serological surveys need not be considered a prerequisite for a vaccination programme.

In the present state of knowledge, there are many questions which cannot be answered. It is not yet known how effective the vaccine will be in a country where the disease is practically restricted to early childhood, nor is it known what effect vaccination will have on the epidemiological situation. Should it be proven that mass vaccination greatly reduces dissemination of poliomyelitis virus in an area, artificial immunity will not be reinforced by " natural " exposure, and the vaccinated population will be immune only for as long as the protection of the vaccine lasts, unless reinforcing doses are given at regular intervals. There is at present no knowledge of the long-term effects of vaccination. The possibility must be considered that in such areas the favourable balance between infection and immunity which at present exists may be upset.

On the other hand, it must be recognized that in recent years many countries in tropical and sub-tropical areas have noted an increase in the incidence of poliomyelitis; and there is reason to believe that poliomyelitis may become a public health problem of major importance in areas where now it is considered of minor importance. It is therefore emphasized that every effort should be made to acquire a better knowledge of the poliomyelitis problem in all countries as soon as possible by the improvement of statistical information and, if necessary, by suitable serological surveys. It should be noted here that in small islands and other isolated communities, serological surveys may be the only way of obtaining a true picture of the situation. Although poliomyelitis virus may only rarely be introduced into such communities, it may cause devastating epidemics when this happens.

Practical problems which face the public health administration in planning a vaccination campaign include such questions as dosage, route of injection, number of injections and the intervals between them, the duration of immunity and the need for reinforcing doses, the probable incidence of complications and their treatment, the control of vaccine production and of the finished product, and its stability under different

conditions of storage, climate, and transport. It is considered undesirable at the present time to attempt to lay down any specifications which might restrict further developments. The following remarks should therefore be considered only as a guide which will certainly have to be modified as experience is accumulated.

Vaccine has been administered intramuscularly, subcutaneously, or intradermally. The optimum dosage schedule has not yet been determined. At the present time, the recommended dose is 1 ml intramuscularly or subcutaneously, or about 0.2 to 0.5 ml intradermally in two sites. The first two doses have usually been given at an interval of about one month and have been followed by a reinforcing dose several months later. Recent experience in the USA suggests that a significant degree of protection may be conferred by a single dose.

The provocation of paralytic poliomyelitis by inoculations, particularly intramuscular inoculations which cause local reactions, seems now to be established. There is no reason to assume that inoculation of poliomyelitis vaccine is completely free from this risk, although its very slight local irritant action may minimize the risk.

The assessment of the risk of provocation, if any, is of importance in deciding whether to carry on mass vaccination campaigns during epidemics of poliomyelitis. Opinions on the probable frequency with which provocation may occur as a result of vaccination vary from zero to relatively high figures, and it is clear that no opinion is fully supported by adequate evidence.

It is recognized that health authorities may be faced with a virtual necessity to carry out mass vaccination of populations threatened with a large epidemic. It is impossible, for the reasons stated, to give clear guidance on the possible dangers of provocation which would, in any case, be set against the benefits of the immunity produced. It is nevertheless essential that health authorities should be aware that the absence of danger has not yet been proven.

It would therefore seem wise to conduct mass vaccination programmes at times when the prevalence of poliomyelitis is usually low. This is recommended if only because of the danger that the chance occurrence of poliomyelitis in a vaccinated child might be ascribed to the vaccine even though the latter may be perfectly safe. Mainly for the reasons mentioned above, it seems inadvisable to vaccinate family contacts of established poliomyelitis cases.

The duration of immunity following vaccination is at present unknown. Neutralizing antibodies may be detected for a few years at least. More information is needed on the relationship between the antibody level and the resistance to infection, but there are grounds for believing that the presence of detectable antibody implies a significant degree of resistance to the paralytic disease.

* * *

In summary, the group considered that, subject to the application of the necessary safeguards, countries with a high incidence of paralytic poliomyelitis should plan to bring vaccination into routine use at an early date. In countries with a low incidence of paralytic poliomyelitis, a decision to vaccinate should be made only after a careful review of the many other factors previously discussed.

Every effort should be made to incorporate in the vaccine strains of virus attenuated as far as possible consistent with the maintenance of adequate antigenicity after inactivation, especially in countries starting vaccine production on a large scale for the first time. If this course were followed, the danger arising from failure to detect traces of residual active virus in the vaccine would be minimized.

Since the production and the testing of poliomyelitis vaccine require considerable experience and the highest technical skill, if accidents are to be avoided, they should be attempted only if technical personnel and equipment of a very high standard are available and only after the technical staff has been thoroughly trained in the essential techniques. In view of the difficulty and expense of meeting this requirement, countries with limited resources might consider some form of co-operation.

The continued successful use of poliomyelitis vaccination, as well as some future developments in this field, may depend on a knowledge of the characteristics of the prevalent poliomyelitis viruses in various parts of the world and of other viruses causing similar clinical syndromes. It is essential, therefore, that national laboratories should co-operate with the existing network of WHO regional poliomyelitis laboratories in order to facilitate the collection, interchange, and study of poliomyelitis viruses, and that laboratories collaborating in the network should also be encouraged to exchange and study viruses which may be responsible for clinical disease resembling poliomyelitis.

OCCUPATIONAL HEALTH

The concept of occupational health has undergone considerable change in the past fifty years, under the combined influence of the increasing importance of industry in the economic, social, and political life of most countries, the impact of industrialization on living and working conditions, and the growing recognition of public responsibility for the health and welfare of the individual. While at the beginning of the century "industrial hygiene" was primarily concerned with occupational diseases and accidents, the aim of "occupational health" today is the protection and improvement of the health of workers of all kinds.

In order to promote a wider understanding of what may be done in this relatively new field of public health and to assist the development of occupational health services in all countries, the WHO Regional Office for Europe organized two seminars, one at Leyden in December 1952, and the other at Milan in October 1953. A recent issue of the *Bulletin of the World Health Organization*[1] contains a selection of the papers presented at these seminars, together with a summary of the seminar discussions. What follows is drawn from the latter.

Medical examinations, job analyses, and placement

Medical examinations in industries are an excellent means of checking on and improving the health of workers and of the population in general. While agreeing on this point, the participants in the Leyden seminar nevertheless felt that not too great an importance should be attached to periodical health examinations. The usefulness of such examinations depends on factors which vary so much from country to country—such as a high frequency of a particular disease, the health standards of the population, the degree of development of public health services and their structure—that no definite rules can be established as to the intervals at which the examinations should be held or of what they should consist. For example, while industrial physicians examine

[1] *Bull. Wld Hlth Org.*, 1955, 13, 491-742

all wage-earners in French industries once a year, in Norway only those under 20 and over 50 years of age are so examined.

At the Leyden meeting, several participants mentioned the more or less marked opposition of the trade unions in certain countries to the principle of pre-employment medical examinations which, according to them, are used for the rejection rather than for the placement of candidates. In order to dissipate this impression and to obtain the co-operation of the trade unions, in several countries, the United Kingdom and Belgium in particular, these medical examinations are given during the three weeks subsequent to engagement.

In discussions on different methods of assessing working capacity, it was decided that a satisfactory system must be sufficiently flexible to make it adaptable to the varying conditions in industry. The seminar participants preferred a system of rating based on candidates' abilities, which experience in the Netherlands has shown to be the most practical approach at the present time.

A worker cannot be considered suitable for a post merely because he has the ability to do the work: the candidate's capacity for adapting himself to the conditions of employment must also be taken into account. Persons with great emotional stability appear to have a particular capacity for adapting themselves, and for this reason they can sometimes be assigned to jobs for which they cannot fulfil all the requirements. It must not be forgotten that a worker is also a member of a team to which he must be able to adapt himself.

There is no doubt that early vocational guidance will make later placement easier. The future worker chooses his occupation on the basis of his capacities and disabilities. This is particularly true of occupations which demand great physical strength, such as lumbering.

Experience has shown that there is no great difficulty in placing workers with slight disability, especially in periods of shortage of labour. On the other hand, job analysis and pre-employment examination are extremely important for the severely disabled. Although it is often difficult to find employment for mentally handicapped persons, persons physically disabled as a result of accidents can be just as efficient as able-bodied workers, provided they are given suitable work. Sickness absenteeism above the average may, however, occur when workers suffering from chronic diseases, such as chronic bronchitis, tuberculosis, or gastric ulcers, are employed, thus disturbing production and increasing the employer's contribution to sickness insurance. It was the general opinion, however, that this extra economic burden would be part of the employer's social responsibility.

Absenteeism in industry

The discussions at both seminars provided interesting information on the problem of absenteeism in several countries. General experience in many countries has shown that only a very small part of total absenteeism is due to occupational diseases. It was also found that absenteeism seems to be less in the smaller than in the larger undertakings.

Both at Leyden and at Milan examples were given showing that economic factors play a very variable role from country to country. In some countries (Belgium, Switzerland) the raising of sickness benefits has brought about an increase in the number of days lost owing to accident or illness, whereas in others (France, Netherlands) it has caused no change.

At the first seminar it was pointed out that the situation of the labour market, and in particular the drop in unemployment, may have contributed to the increase in absenteeism in industry.

On the subject of records and statistics of absenteeism, the participants at both seminars

considered that it would be desirable to adopt a uniform system so that data for industries within one country or in different countries would be comparable. It was emphasized at Leyden that it is the industrial physician who is responsible for keeping or supervising statistics on absenteeism.

The problem of absenteeism is still far from being solved, and the hope was expressed that investigation of its causes would continue and that a comparative study would be made of the differences in absenteeism in different countries among groups of workers of the same age, of the same occupation, and employed in the same type of industry.

Mental health of workers

In the opinion of participants in the Milan seminar, the question of the mental health of workers, to which very little attention has so far been paid, is destined to become one of the most important problems of occupational health. For adequate protection of the mental health of workers, three of their essential needs must be satisfied, and these were defined by the participants as follows:

(1) the need to create and to do useful work;

(2) the need to feel themselves respected;

(3) the need for security.

It was agreed that it is easier to apply the principles of mental health in large industries if work groups do not exceed 300-500 persons and if they are decentralized and enjoy a certain amount of independence.

It was also recognized that mental health in industry depends upon the adaptation of each worker to his task and on human relations in the undertaking, as well as on economic and social factors. Industrial medical officers must therefore not only detect at an early stage any case of maladjustment to work, but also contribute to the creation of a spirit of understanding among the various groups of workers.

A number of adaptation problems connected with recruitment and promotion were discussed at the Leyden seminar. It sometimes happens that a post is filled not on the basis of the work requirements, but on that of the ability and qualifications of the last holder of the post. Sometimes insufficient care is taken to ascertain the real abilities of a candidate, which leads to the recruitment of over-qualified or under-qualified persons.

At Milan it was pointed out that alcoholism constitutes a serious problem in some countries. The suggestion was also made that female labour, by disorganizing family life, might have a bad effect on the mental health of a large part of the population. The presence of a wife in the home was considered to be an important stabilizing factor, but it was also realized that without female labour many countries would be unable to maintain the living standards they have achieved.

Problem of elderly workers

It was pointed out at Leyden that the employment of elderly workers depends not only on individual physiological and psychological factors, but also on the labour market and on the demographic situation in each country. In Germany, older workers have no difficulty in finding employment, owing to the loss of man-power due to the war and to the low birth-rate since 1942. In the Netherlands, on the other hand, where the birth-rate has risen considerably, very few industries will employ many workers over 50 years of age; it is considered there that in the heavy industries only 75% of workers over 50 are still capable of " normal " work. Persons of advanced age need to be active, and studies on output and absenteeism

show that their employment is justified. Nevertheless, the continual increase in the proportion of older workers is creating a serious problem in industry. In 1980 the USA will probably have 22 million persons over 65 years of age, and 43 million between 45 and 64.

Retention of older workers seems to be most easily feasible in agriculture, while the greatest difficulties are met with in the small industries, which offer fewer opportunities to change occupation.

It was felt that a study should be made of the reasons for workers' desiring to continue in employment after the normal retiring age. In Ireland it has been found that workers generally retire at the specified age if their pension is adequate or if they intend to engage in some other remunerative work or occupy themselves with some hobby. Investigations in Norway have shown that half, and possibly two-thirds, of the men want to continue work, even though some of them are not fit for it.

The seminar expressed the hope that a more thorough study would also be undertaken of the physical and mental aptitudes of older workers and of the best way of utilizing such workers without detriment to their health. It was felt that comparison of data collected in different countries would be considerably facilitated if the work to be done could be based on a co-ordinated plan of research.

Rehabilitation of physically handicapped workers

The success of any rehabilitation technique depends on the extent of the disability and on the age of those to whom it is applied. Experience has shown that rehabilitation is more difficult after the age of 40 or when the handicap is due not to illness but to an accident.

The question of applying a system of compulsory employment of a certain percentage of handicapped workers (e.g., 3% in the United Kingdom, and 6% in Germany) was considered by seminar participants as too rigid, since some sectors of industry can absorb more such workers than others. Such a provision is superfluous where rehabilitation programmes are successfully applied.

At the first seminar, the discussion centred mainly on the problem of the rehabilitation of tuberculous workers, for whom great efforts are made in a number of countries. The Irish Red Cross has recently set up two workshops for the rehabilitation and training of tuberculous workers before their re-entry into industry. In the United Kingdom, when a tuberculous person is capable of part-time work only, the national insurance will provide for the rest of his wages through the public assistance board. Statistics from the Philips' factories in the Netherlands show that 36% of 1307 workers taken on as cured of tuberculosis between 1935 and 1948 had a relapse.

There are a great many difficulties in connexion with the rehabilitation of temporary invalids, and quite often workers, employers, and even physicians oppose it. They should all be informed of the advantages of early return to work. For the worker this is better than sickness benefits and prolonged treatment because it prevents him from becoming frustrated and keeps him in good physical and mental condition; as for the employer, it lessens his contribution to the sickness fund and reduces absenteeism.

Rehabilitation of persons who have suffered minor accidents does not necessarily require special centres. Industrial medical services, with the aid of technical sections, should be sufficient, as will be seen from the figures below on the treatment of persons for accident or injury in a ball-bearing plant in Sweden.

Year	Total number of workers	Accidents treated at the plant		Accidents compensated		Number of days sick leave per compensated accident
		total number	per 100 workers	total number	per 100 workers	
1947	3 950	1 692	42.8	309	7.8	21.0
1948	4 570	2 305	50.6	324	7.0	20.5
1949	4 590	2 049	44.9	316	6.9	23.0
1950	4 398	1 686	38.2	223	5.1	21.3
1951	4 260	1 504	35.2	149	3.5	25.4

In this plant, 82%-90% of the injured are back at work within two days; if they are absent for longer, they have the right, under national legislation, to compensation for occupational accident. The medical officers of the plant, in agreement with the heads of the various workshops, decide what type of work can be temporarily assigned to an injured employee.

Safety of workers

At the Milan seminar it was recognized that the frequency of industrial accidents constitutes an important problem. In France alone, among six million workers covered by social security, some 1 800 000 persons annually suffer occupational accidents, of whom 3000 die, 70 000 are permanently disabled, and 100 000 are temporarily disabled.

The prevention of accidents is a collective responsibility, shared not only by workers and employers, but also by industrial medical officers, psychologists, safety engineers, and social workers. The human factor is an important cause of accidents and requires appropriate action, but technical preventive measures must not be neglected. By organizing work with due regard to human physiology and psychology, the number of accidents may be reduced.

It is extremely difficult to enforce safety rules. Persuasion is more effective than compulsion, and excellent results are obtained by enlisting the good offices of trade union representatives or of volunteers among the workers. It is doubtful whether posters are of much use in preventing accidents; several seminar participants considered them even to have a bad effect.

There is an educational aspect to the prevention of accidents. Medical officers and engineers should be taught safety principles. The education of workers, and in particular of new workers, also gives good results. In Belgium it is largely due to the safety committees, which have existed in some industries for as long as 25 years, that the rate of accidents has dropped by 60%.

It cannot be said that all categories of staff pay the same amount of attention to safety measures and accident prevention. A study made in France showed that manual workers, on the whole, attach great importance to them, but that the higher the professional category the less is the attention given to them.

Health services in large plants

In examining this question, the participants in both seminars discussed whether treatment and medical care should be part of the responsibility of medical services in large plants. In the course of the discussions, both those for and those against purely preventive industrial health services developed their arguments. The former maintained that most sickness among workers has its origin outside their occupation and that, moreover, the treatment of diseases and injuries is the same whether they are of occupational origin or not. Therefore, the public health or social security organizations should be responsible for treatment, and the real problem is how to co-ordinate the activities of these bodies with those of the industrial medical

officer. Those opposed to this view pointed out that it is difficult to dissociate prevention and treatment altogether and maintained that preventive medicine and curative medicine are not separate but complementary.

In France, for instance, treatment by industrial medical officers is limited to first aid. In Morocco, the mining companies, on account of their isolation, find it preferable to organize medical treatment services as well as industrial health services proper. A number of large undertakings in Belgium have set up, within the framework of the industrial health service, special hospitals for the treatment of injured workers.

At the Milan seminar it was suggested that liaison might be maintained between the medical services in large factories and the university institutes of industrial health. It was felt that even if the contacts were limited to exchange of information, both parties might draw great benefit from such liaison.

Health services in small plants

At Milan it was pointed out that, although the problem of treatment in the factory has still to be solved, it might be an advantage in small plants for part of the medical treatment to be entrusted to the plant physician, even if only to keep the worker at his job.

Liaison between the plant physician and the general medical practitioner, on the one hand, and the local public health services, on the other, is particularly important in relation to smaller plants.

Nurses attached to the health service in small plants play a very important role, and they should not be overloaded with administrative tasks. A survey made in 12 small industrial undertakings in the USA revealed that industrial nurses spend 22% of their time on work which does not properly fall within the purview of their profession.

From the discussions at Leyden it was clear that health problems differ in many ways between large and small plants. The accident rate in the latter is often higher; and, in general, hygiene conditions call for improvement. On the other hand, in small plants, neuroses are less common, nervous and mental disorders are less serious, and the general morale is better. As a result, there is also less absenteeism. Small plants, however, offer fewer opportunities for rehabilitation, reclassification, and transfer of workers. A group of plants in the same area of the Netherlands have solved this problem by agreeing that, if the industrial medical officer of their common health service so advises, any worker in one plant may be transferred to another plant within the group.

At Leyden reference was made to the desirability of obtaining the agreement not only of administrations of undertakings, but also of the trade unions with regard to the establishment of health services. Some participants did not consider trade union health services to be either effective or practical.

It was proposed, also at Leyden, that a pilot study be undertaken in various countries on health services in small plants, in order to define their problems and duties, establish appropriate methods and techniques, and co-ordinate their activities with those of the public health services.

* * *

The WHO-sponsored seminars in Leyden and Milan threw considerable light on a number of occupational health problems and drew attention to others which may warrant further discussion at the international level, among them the training of those who are bound to play a part in occupational health. Professor E. C. Vigliani, in particular, pointed out at the Milan seminar that occupational health calls not only for specialized training of some physicians, but also for proper orientation of the general practitioner:

> There are today thousands of physicians whose time is devoted fully or in part to medical work in

industry, and it is proposed on every hand to enlarge their field of activity by legislative measures. Only a certain number of them, however, have so far received the proper training. Moreover, most general practitioners have a large number of workers in industry or trade among their patients. Under these conditions, if we wish to protect the health of the workers properly and to care for them, and to develop industrial medical services to that end, we must give every medical student some knowledge—no matter how summary—of the effect of work on health. We must also give the qualified physician the opportunity not only to keep up to date with developments, but also to engage in more advanced study and to undertake scientific research in this branch of medicine.

MORTALITY FROM ULCERS OF THE STOMACH AND DUODENUM

Statistics assembled by WHO and made available in a study published by the Organization [1] reveal that, at least in most of the countries covered in the study, ulcers of the stomach and duodenum are responsible for more deaths than cirrhosis of the liver, bronchitis, non-epidemic influenza, and other common infectious diseases.

The Sixth Revision of the International Lists of Diseases and Causes of Death, which was adopted in 1948, is now used in many countries. The Detailed List classifies gastric and duodenal ulcers under two separate headings, but the two are given under a single heading in the Abbreviated List of 50 Causes for Tabulation of Mortality, which is used for certain official statistics. Even the statistics which are established on the basis of the Detailed List have a probable margin of error since some members of the medical profession continue to use the term " gastric ulcer " whatever the anatomical location, which it is not always possible to specify in any case.

With this qualification, it may be noted in Table I, which shows considerable variations according to country, that the crude mortality rate for ulcers is about 7 deaths per 100 000 of the population for both sexes, and that death from this cause is, in general, three to four times as great among males as among females.

It is interesting to consider the mortality rates for different age groups for the two

TABLE I. MORTALITY FROM ULCERS OF THE STOMACH AND DUODENUM FOR ALL AGES, PER 100 000 OF THE POPULATION, 1951-1953

Country	Both sexes	Male	Female
Canada	5.0	8.1	1.9
USA	5.7	9.2	2.2
Ceylon	2.0	1.9	2.1
Japan	20.1	29.0	11.6
Germany (Federal Republic)	6.9	12.0	2.4
West Berlin	8.9	17.1	2.9
Austria	8.0	12.6	4.0
Denmark	7.4	11.4	3.5
Finland	4.8	7.9	2.0
France	3.2	5.3	1.2
Ireland	8.2	12.1	4.1
Italy	6.3	10.8	2.0
Norway	4.0	5.4	2.6
Netherlands	5.2	8.2	2.2
England and Wales	12.2	19.1	5.9
Scotland	11.9	19.0	5.3
Northern Ireland	7.6	11.5	4.0
Sweden	8.7	13.2	4.2
Switzerland	6.8	9.5	4.3
Australia	7.2	11.2	3.2
New Zealand	8.0	12.2	3.7

[1] *Epidem. vital Statist. Rep.*, 1955, **8**, 359

TABLE II. INDEX OF INCREASE OF MORTALITY FOR BOTH TYPES OF ULCERS FROM AGE 40-49 (40-49 = 100)

	40-49	50-59	60-69	70-79	80 & +
Canada	100	228	434	766	1123
USA	100	224	406	589	789
Japan	100	236	469	680	678
Germany (Federal Republic)	100	180	223	315	323
Austria	100	210	417	620	880
Denmark	100	239	333	593	736
Finland	100	180	348	373	347
France	100	168	262	400	344
Ireland	100	157	263	348	257
Italy	100	152	155	203	191
Norway	100	247	350	720	1213
Netherlands	100	252	396	656	942
England and Wales	100	240	499	827	1194
Scotland	100	212	345	619	879
Northern Ireland	100	317	633	983	1879
Sweden	100	232	383	667	1058
Switzerland	100	224	467	991	1478
Australia	100	266	502	830	1214
New Zealand	100	265	533	1198	1849

types of ulcer, as shown in Table II, in which the age group 40-49 years is taken as the basis of comparison. The influence of the "age factor" is seen to be a definite and sometimes very important one.

According to figures which are not reproduced here, duodenal ulcers cause slightly greater mortality among young men than do stomach ulcers; the latter, on the other hand, cause far more deaths among old people. For reasons previously mentioned, however, the relative rates may appear greater than they actually are. Some of the published data on the two types of ulcer are summarized in Table III.

Study of the detailed figures of mortality according to sex and age reveals that death from ulcers is higher among men at an earlier age than among women, but that with increasing age the difference becomes less.

It would, of course, be unwise to take the published statistics at their face value, regardless of how much care has been taken in

TABLE III. PERCENTAGE OF DEATHS FROM ULCERS OF THE STOMACH OR OF THE DUODENUM COMPARED WITH TOTAL ULCER DEATHS

(deaths from both types = 100)

		Males %	Females %
Canada	Stomach	53	62
	Duodenum	47	38
USA	Stomach	51	58
	Duodenum	49	42
Japan	Stomach	92	92
	Duodenum	8	8
Germany	Stomach	71	81
	Duodenum	29	19
France	Stomach	89	92
	Duodenum	11	8
Italy	Stomach	59	68
	Duodenum	41	32
Netherlands	Stomach	51	67
	Duodenum	49	33
England and Wales	Stomach	48	67
	Duodenum	52	33
Sweden	Stomach	54	68
	Duodenum	46	32
Australia	Stomach	57	69
	Duodenum	43	31

assembling them. Any comparison of mortality rates between one country and another would not be warranted unless precise knowledge of how the figures were gathered and drawn up were available. On the other hand, comparisons made from one year to another for a given country can generally be considered valid, provided that any legislative or administrative changes which have been introduced during the periods covered are taken into account. The data published on ulcers of the stomach and duodenum, which deal mostly with the period 1949-53, offer an opportunity for such a study.

World Health Day, 7 April 1956

Announcement has been made that the theme selected for World Health Day in 1956 is the struggle against the insect-borne diseases. The slogan suggested for expression of this theme is " Destroy disease-carrying insects ". Each country should direct attention to the insect-borne diseases which are of particular importance within its borders, and to the international as well as the national efforts for their control.

In preparation for observance of World Health Day, suitable publicity material, consisting of a series of twelve articles on relevant subjects, by contributors of note, is being supplied to governments requesting it. This material is available in either English or French.

World Health Day is being more widely observed each year, and it is hoped that this year will see an even greater number of governments participating in this effort to develop an informed public opinion on matters of health.

Tariffs of Sanitary Charges

A supplement to the *Weekly Epidemiological Record* (1955, No. 46, Supp. 5) gives information on the tariffs of sanitary charges in force in 65 countries and territories on 18 November 1955. Among the items included are charges for deratting, disinsecting, or disinfection of ships and aircraft, inspection for the purpose of deratting exemption, isolation of passengers, vaccinations, quarantine fees, measures in connexion with the Mecca Pilgrimage, and others. Also given is a statement showing the position of countries and territories under the International Sanitary Regulations, listing them as bound without reservation, bound with reservation, or not bound.

This supplement will serve as a useful guide to shipping agencies, captains of ships and aircraft, health administrations, and individuals undertaking an international voyage.

Notes and News

WHO-Sponsored Visit of Medical Scientists to Egypt

A group of eminent medical scientists from a number of countries paid a month-long visit to Egypt late in 1955, under the auspices of WHO as part of its exchange of information programme.

Chairman of the group was Dr Corneille Heymans, Professor of Pharmacology at the University of Ghent, Belgium. Other members were: Dr F. A. E. Crew, University of Edinburgh, Scotland (Professor of Public Health and Social Medicine); Dr E. W. H. Cruickshank, University of Aberdeen, Scotland (Professor of Physiology); Dr G. Fanconi, University of Zurich, Switzerland (Professor of Paediatrics); Dr E. Grzegorzewski, Director, Division of Education and Training Services, WHO; Dr E. Husfeldt, University of Copenhagen, Denmark (Professor of Surgery); Professor L. Kreyberg, University of Oslo, Norway (Professor of Pathology); Dr C. McEwen, Dean of New York University College of Medicine, New York, USA (Associate Professor of Medicine); Dr O. Secher, University Hospital, Copenhagen, Denmark (Reader in Anaesthesiology); and Dr H. de Watteville, University of Geneva, Switzerland (Professor of Obstetrics and Gynaecology).

The visiting group gave lectures, presented scientific films, worked in hospital departments with their Egyptian colleagues of the Cairo and Alexandria Universities, and participated in conferences and discussions on specific subjects and on medical education in general.

Malaria-Control Programme Planned for Sudan

A WHO consultant, Dr A. B. Gilroy, principal of the India Branch of the Ross Institute of Tropical Hygiene, Assam, has been sent to Sudan to advise the Ministry of Health concerning its malaria-control policy. The Government has already done impressive work in controlling malaria but contemplates intensification of its efforts, with WHO aid, because of danger of an increase in the prevalence of the disease as a result of an irrigation project in the Blue Nile Province.

Dr Gilroy's assignment is the first step in WHO assistance. It is expected that a malaria-control team will begin work in Sudan early in 1956.

Trachoma Survey in Jordan

Dr Farid Abdin, ophthalmic surgeon at the Memorial Ophthalmic Laboratory, Giza, Egypt, has been appointed by WHO to carry out a survey of trachoma in Jordan. He will visit all parts of the country, examining patients and gathering statistics on the incidence of trachoma. Subsequently, on the basis of his findings he will help the Ministry of Health in initiating a WHO-aided trachoma-control project and will discuss the organization and equipping of a hospital for eye diseases in Jordan.

Training of Auxiliary Health Personnel in Libya

Dr Ahmed Gamaleddin el Hefny, a public health administrator of long experience in Egypt, has been appointed by WHO to head a team which will help to develop a training programme for auxiliary health personnel at a new school in Benghazi, Libya. The international team will also include a sanitarian and a nurse. The Organization plans to give assistance to this project for two years, beginning in 1956.

Meeting of Fellowship Administrators

More WHO fellows study in Europe than in any other region. Medical and adminis-

trative officers from five countries in Europe (France, Netherlands, Sweden, Switzerland, and the United Kingdom) which receive large numbers of WHO fellows for post-graduate study met informally with WHO officials in Geneva from 14 to 16 December to discuss the day-to-day placement problems arising out of the WHO fellowship programme. During the discussions, progress was made on such practical points as advance information on fellows, planning of individual study and of group training, placement in research and training institutes, and language difficulties.

Heart Operations

The development of the congenital heart disease centres in Vienna and Zagreb since the visit of a WHO expert team in 1950 [1] has now been reviewed. In Vienna, 150 children with congenital heart malformations, including 82 " blue babies ", have been operated on (only four operations were fatal). Eighty operations on adults have also been performed. In Zagreb, about 500 children have been examined. Since 1951, 80 heart operations on children (mortality: four cases) and 67 heart operations on adults (mortality: three cases) have been performed.

As was expected, there was at first a certain accumulation of cases in both centres. At present, about 100 cases are seen annually in Zagreb, and 30 to 40 cases among children are seen annually in Vienna.

Seminar on the Teaching of Preventive Medicine

The first of two seminars on the teaching of preventive medicine,[2] organized by the Pan American Sanitary Bureau (PASB), which acts as WHO Regional Office for the Americas, was held in Viña del Mar, Chile, from 10 to 15 October 1955. It was attended by 73 participants from Argentina, Bolivia, Brazil, Chile, Paraguay, Peru, Uruguay, and Venezuela, as well as by representatives of the Rockefeller Foundation, the Institute of Inter-American Affairs, WHO, and the PASB. Dr Alejandro Garretón Silva, Dean of the Faculty of Medicine of the University of Chile, was elected Chairman; and Dr Myron Wegman, Chief of the Division of Education and Training of the PASB, acted as Secretary-General of the seminar.

A second seminar on the same subject is expected to be held in 1956 in Mexico, and will be for participants from Colombia, Cuba, the Dominican Republic, Ecuador, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama, Puerto Rico, and Surinam.

[1] See *Chron. Wld Hlth Org.*, 1951, 5, 78.

[2] See *Chron. Wld Hlth Org.*, 1955 9, 182.

Review of WHO Publications

Bulletin of the World Health Organization, 1955, Volume 13, Number 5 (pages 743-936)

In addition to articles on rabies prophylaxis and on Q fever which have been the subject of more detailed consideration in previous issues of the *Chronicle*,[1] this number of the *Bulletin* contains two papers on serology (" Serological findings in leprosy and tuberculosis with the Wassermann, Meinicke, and VDRL tests ", by H. Ruge, and " Nouvelle technique de fixation du complément dans la sérologie de la syphilis ", by G. M. P. Roulin) and two on biological standardization (" The International Standard for Oxytetracycline ", by J. H. Humphrey, J. W. Lightbown, M. V. Mussett & W. L. M. Perry, and " The International Standard for Thyrotrophin ", by M. V. Mussett & W. L. M. Perry). Also in this number is a bibliographical section on yellow fever and cholera.

Bulletin of the World Health Organization, 1955, Volume 13, Number 6 (pages 937-1207).

This number of the *Bulletin* is devoted to a variety of studies.

There is the second of a series of articles on the chemical, pharmacological, therapeutic, and addictive properties of synthetic drugs with morphine-like effect, by O. J. Braenden, N. B. Eddy & H. Halbach. It deals with the structural characteristics of such substances in relation to their analgesic action. This series of articles is being published in accordance with a resolution of the United Nations Economic and Social Council inviting WHO to provide technical information on synthetic narcotics.

Maria E. Alessandrini describes a practical method developed for taking samples of DDT or other insecticides from treated surfaces so that the content of insecticide in the residue can be analysed. This method is based on use of parchment paper coated with a silicone preparation to which the DDT adheres.

The results of a serological survey made in Thailand in the course of a yaws-control programme aided by WHO and UNICEF are summarized and discussed by J. M. F. D'Mello & P. Krag. Approximately 3500 persons suffering from yaws were subjected to serological examination before being treated. Cases with recent lesions as well as those with plantar and palmar hyperkeratosis gave a high rate of seropositivity, while cases with bone and joint lesions and latent cases gave a considerable degree of seronegativity. One year after treatment with PAM, there were no signs of active yaws in those treated. A reversion to seronegativity was noted in only 11% of cases, however.

A sample survey of tuberculosis prevalence in Japan in 1953, reported by Masayoshi Yamaguchi, revealed a morbidity rate which calls for a revision of tuberculosis-control programmes in that country.

This number of the *Bulletin* is concluded with the sixth of Dr R. Pollitzer's studies on cholera, the subject being the pathology of the disease.

A bibliographical section contains references on smallpox.

[1] *Chron. Wld Hlth Org.*, 1955, 9, 308-335

International Non-Proprietary Names for Pharmaceutical Preparations

There is need to avoid the confusion which exists when different non-proprietary names come into use for the same medicinal substance. This multiplicity of names can be the source of difficulties in the daily work of the physician and of the pharmacist, as well as in therapeutic research throughout the world.

In many countries attempts have been made and progress achieved in obtaining the desired uniformity on a national level (examples: " Generic Names " of the Council on Pharmacy and Chemistry of the American Medical Association, " Approved Names " of the General Medical Council in the United Kingdom, " Nordiske Farmakopenaevn " of the Scandinavian Pharmacopoeia Council, " dénominations communes " in France, etc.). The World Health Organization was asked to co-ordinate these efforts at an international level, and special requests were also made to select international non-proprietary names for the drugs liable to produce addiction in order to facilitate their international control.

According to the following " Procedure for the selection of recommended International Non-Proprietary Names for pharmaceutical preparations ", WHO receives requests for the establishment of international non-proprietary names for new pharmaceutical preparations which can be used freely in all countries, and publishes lists of proposed international non-proprietary names and of recommended international non-proprietary names.

PROCEDURE FOR THE SELECTION OF RECOMMENDED INTERNATIONAL NON-PROPRIETARY NAMES FOR PHARMACEUTICAL PREPARATIONS [1]

The following procedure shall be followed by the World Health Organization in the selection of recommended international non-proprietary names for pharmaceutical preparations, in accordance with the World Health Assembly resolution WHA3.11:

1. Proposals for recommended international non-proprietary names shall be submitted to the World Health Organization on the form provided therefor.

2. Such proposals shall be submitted by the Director-General of the World Health Organization to the members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations

[1] The amended text reproduced here was adopted by the Executive Board in resolution EB15.R7 and supersedes that adopted by the Board at its twelfth session (see *Official Records* No. 49, Annex 6).

designated for this purpose, for consideration in accordance with the " General principles for guidance in devising International Non-proprietary Names ", appended to this procedure. The name used by the person discovering or first developing and marketing a pharmaceutical preparation shall be accepted, unless there are compelling reasons to the contrary.

3. Subsequent to the examination provided for in article 2, the Director-General of the World Health Organization shall give notice that a proposed international non-proprietary name is being considered.

A. Such notice shall be given by publication in the *Chronicle of the World Health Organization* and by letter to Member States and to national pharmacopoeia commissions or other bodies designated by Member States.

(i) Notice may also be sent to specific persons known to be concerned with a name under consideration.

B. Such notice shall:

(i) set forth the name under consideration;

(ii) identify the person who submitted a proposal for naming the substance, if so requested by such person;

(iii) identify the substance for which a name is being considered;

(iv) set forth the time within which comments and objections will be received and the person and place to whom they should be directed;

(v) state the authority under which the World Health Organization is acting and refer to these rules of procedure.

C. In forwarding the notice, the Director-General of the World Health Organization shall request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the proposed name during the period it is under consideration by the World Health Organization.

4. Comments on the proposed name may be forwarded by any person to the World Health Organization within four months of the date of publication, under article 3, of the name in the *Chronicle of the World Health Organization.*

5. A formal objection to a proposed name may be filed by any interested person within four months of the date of publication, under article 3, of the name in the *Chronicle of the World Health Organization.*

A. Such objection shall:

(i) identify the person objecting;
(ii) state his interest in the name;
(iii) set forth the reasons for his objection to the name proposed.

6. Where there is a formal objection under article 5, the World Health Organization may either reconsider the proposed name or use its good offices to attempt to obtain withdrawal of the objection. Without prejudice to the consideration by the World Health Organization of a substitute name or names, a name shall not be selected by the World Health Organization as a recommended international non-proprietary name while there exists a formal objection thereto filed under article 5 which has not been withdrawn.

7. Where no objection has been filed under article 5, or all objections previously filed have been withdrawn, the Director-General of the World Health Organization shall give notice in accordance with subsection A of article 3 that the name has been selected by the World Health Organization as a recommended international non-proprietary name.

8. In forwarding a recommended international non-proprietary name to Member States under article 7, the Director-General of the World Health Organization shall:

A. request that it be recognized as the non-proprietary name for the substance; and

B. request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the name, including prohibiting registration of the name as a trade-mark or trade-name.

GENERAL PRINCIPLES FOR GUIDANCE IN DEVISING INTERNATIONAL NON-PROPRIETARY NAMES

1. Names should, preferably, be free from any anatomical, physiological, pathological or therapeutic suggestion.

2. An attempt should first be made to form a name by the combination of syllables in such a way as to indicate the significant chemical groupings of the compound and/or its pharmacological classification. Preference should be given to the following syllables:

Latin	English	French	
inum	ine	ine	for alkaloids and organic bases
inum	in	ine	for glycerides and neutral principles
olum	ol	ol	for alcohols and phenols (-OH group)
alum	al	al	for aldehydes
onum	one	one	for ketones and other substances containing the CO group
enum	ene	ène	for unsaturated hydrocarbons
anum	ane	ane	for saturated hydrocarbons
cainum	caine	caïne	for local anaesthetics
mer	mer	mer	for mercurial compounds
sulfonum	sulfone	sulfone	for sulfone derivatives
quinum	quine	quine	for antimalarial substances containing a quinoline group
crinum	crine	crine	for antimalarial substances containing an acridine group
sulfa	sulfa	sulfa	for derivatives of sulfanilamide
dionum	dione	dione	for anti-epileptics derived from oxazolidinedione
toinum	toin	toïne	for anti-epileptics derived from hydantoin
stigminum	stigmine	stigmine	for anticholinesterases

3. Names should be distinctive in sound and spelling. They should not be inconveniently long and should not be liable to confusion with names already in use.

4. The addition of a terminal capital letter or number should be avoided as far as possible.

5. Names proposed by the person discovering or first developing and marketing a pharmaceutical preparation, or already officially adopted in any country, or used in the national pharmacopoeias, or in works of reference such as " New and Non-official Remedies ", should receive preferential consideration.

* * *

In accordance with article 3 of the Procedure for the Selection of Recommended International Non-Proprietary Names for Pharmaceutical Preparations, notice is hereby given that the following names are under consideration by the World Health Organization as Proposed International Non-Proprietary Names.

Comments on, or formal objections to, these proposed names may be forwarded by any person to the World Health Organization within four months from 1 February 1956.

The inclusion of a name in this list does not imply any recommendation for the use of the substance in medicine or pharmacy.

PROPOSED INTERNATIONAL NON-PROPRIETARY NAMES (*Prop. I.N.N.*): LIST 4 [2]

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
acetarsolum acetarsol	3-acetamido-4-hydroxyphenylarsonic acid
acetylcholini chloridum acetylcholine chloride	2-acetoxyethyltrimethylammonium chloride

[2] Other lists of proposed international non-proprietary names will be found in *Chron. Wld Hlth Org.*, 1953, **7**, 297; 1954, **8**, 216, 313. A list of recommended international non-proprietary names was published in *Chron. Wld Hlth Org.*, 1955, **9**, 185.

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
acidum ascorbicum ascorbic acid	3-oxo-L-gulofuranolactone (enolic form)
acidum folicum folic acid	*N*-[4′-({[2-amino-4-hydroxy-6-pteridyl]methyl}amino) benzoyl]-L (+)glutamic acid
acidum iophenoicum iophenoic acid	α-(3-hydroxy-2,4,6-triiodobenzyl)-butyric acid
acidum nicotinicum nicotinic acid	pyridine-3-carboxylic acid
adipiodonum adipiodone	adipic acid bis-(2,4,6-triiodo-3-carboxyanilide)
aethisteronum ethisterone	17α-ethynyl-17β-hydroxy-3-oxoandrostene-4
aethylis biscoumacetas ethyl biscoumacetate	ethyl 4,4′-dihydroxy-3,3′-dicoumarinylacetate
amidopyrinum amidopyrine	2,3-dimethyl-4-dimethylamino-1-phenyl-5-pyrazolone
aminitrozolum aminitrozole	2-acetamido-5-nitrothiazole
aminophyllinum aminophylline	mixture of theophylline and ethylenediamine
aminopterinum natricum aminopterin sodium	sodium 4-aminofolate
amphetaminum amphetamine	(±) 2-amino-1-phenylpropane
androstanolonum androstanolone	3α-hydroxy-17-oxoandrostane
arsthinolum arsthinol	2-(3′-acetamido-4′-hydroxyphenyl)-1,3-dithia-2-arsa-4-*cyclo*pentyl-methanol
atropini methonitras atropine methonitrate	(±) 8-methyl-3-tropoyloxytropane nitrate
barbitalum barbital	5,5-diethylbarbituric acid
barbitalum natricum barbital sodium	sodium salt of 5,5-diethylbarbituric acid
benzatropini methanesulfonas benzatropine methanesulfonate	tropine benzhydryl ether methanesulfonate
bromazinum bromazine	2-(4-bromophenyl-phenylmethoxy)-ethyldimethylamine
buclizinum buclizine	1-(4-chlorobenzhydryl)-4-(4-*tert.*butylbenzyl)-piperazine
butacainum butacaine	3-dibutylaminopropyl *p*-aminobenzoate
butalbitalum butalbital	5-allyl-5-*iso*butylbarbituric acid

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
calciferolum calciferol	
calcii saccharas calcium saccharate	calcium D-glucarate
carbacholum carbachol	carbamoylcholine chloride
carbarsonum carbarsone	4-ureidophenylarsonic acid
carbimazolum carbimazole	2-ethoxycarbonylthio-1-methylimidazole
carbinoxaminum carbinoxamine	2-dimethylaminoethoxy-2-pyridyl-4-chlorophenylmethane
carzenidum carzenide	4-carboxybenzenesulfonamide
cetomacrogolum 1000 cetomacrogol 1000	polyethylene glycol 1000 monocetyl ether
chiniofonum chiniofon	mixture of four parts by weight of 7-iodo-8-hydroxyquinoline-5-sulfonic acid and one part of sodium bicarbonate
chlorbetamidum chlorbetamide	*N*-(2,4-dichlorobenzyl)-*N*-(dichloroacetyl)-ethanolamine
chlormerodrinum chlormerodrine	(3-chloromercuri-2-methoxypropyl)-urea
chlorobutanolum chlorobutanol	1,1,1-trichloro-2-methylpropanol-2
chlorocresolum chlorocresol	6-chloro-3-hydroxytoluene
chloroquinum chloroquin	7-chloro-4-(4′-diethylamino-1′-methylbutylamino)-quinoline
chlorphenaminum chlorphenamine	1-(*p*-chlorophenyl)-1-(2-pyridyl)-3-dimethylaminopropane
chlortetracyclinum chlortetracycline	10-chloro-1-dimethylamino-1,4,6,11,12,13,14,18-octahydro-2,5,711,14-pentahydroxy-4,6-dioxo-11-methylnaphthacene-3-carbonamide
cholini chloridum choline chloride	2-hydroxyethyltrimethylammonium chloride
conessinum conessine	an alkaloid obtained from the seeds of *Holarrhena antidysenterica* L.
cycriminum cycrimine	1-phenyl-1-*cyclo*pentyl-3-piperidino-1-propanol
desoxycortonum desoxycortone	21-hydroxy-3,20-dioxopregnene-4
dibrompropamidinum dibrompropamidine	1,3-bis-(4-amidino-2-bromophenoxy)-propane
dichloroxylenolum dichloroxylenol	2,4-dichloro-3,5-dimethylphenol

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
diethylstilboestrolum diethylstilboestrol	*trans*-3,4-bis-(4-hydroxyphenyl)-hexene-3
digoxinum digoxin	glycoside obtained from the leaves of *Digitalis lanata* Ehrh.
dihexyverinum dihexyverine	2-piperidinoethyl 1-*cyclo*hexyl*cyclo*hexanecarboxylate
dihydralazinum dihydralazine	1,4-dihydrazinophthalazine
dimazolum dimazole	2-dimethylamino-6-(2-diethylaminoethoxy)-benzothiazole
diphemanili methylsulfas diphemanil methylsulfate	*N,N*-dimethyl-4-piperidylidene-diphenylmethane methylsulfate
dithranolum dithranol	1,8,9-anthratriol
ectylurea ectylurea	2-ethylcrotonylurea
edrophonii chloridum edrophonium chloride	ethyldimethyl-3-hydroxyphenylammonium chloride
ergometrinum ergometrine	an alkaloid obtained from ergot
ergotaminum ergotamine	an alkaloid obtained from ergot
erythromycinum erythromycin	an antibiotic produced by a strain of *Streptomyces erythreus*
ethaverinum ethaverine	6,7-diethoxy-1-(3′,4′-diethoxybenzyl)-isoquinoline
gitalinum amorphum gitalin amorphous	a glycosidal principle of *Digitalis purpurea* L.
glycerolum glycerol	propanetriol
heparinum heparin	sodium salt of a complex organic acid having the characteristic property of delaying the clotting of blood
hexylcainum hexylcaine	1-*cyclo*hexylamino-2-propyl benzoate
hydroxystilbamidinum hydroxystilbamidine	1-(4-amidino-2-hydroxyphenyl)-2-(4-amidinophenyl)-ethene
isophanum insulinum isophane insulin	a sterile suspension of insulin with the isophanic equivalent of protamine and zinc chloride
lanatosidum C. lanatoside C	glycoside obtained from the leaves of *Digitalis lanata* Ehrh.
laudexii methylsulfas laudexium methylsulfate	decamethylene-*w*-bis-[1-(3′,4′-dimethoxybenzyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2,2-dimethylisoquinolinium sulfate]

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
levorphanolum* levorphanol	(-) 3-hydroxy-*N*-methylmorphinan
levothyroxinum natricum levothyroxine sodium	L-β-[(4-hydroxy-3,5-diiodophenoxy)-3,5-diiodophenyl]-alanine
lobelinum lobeline	L-2-(2-hydroxy-2-phenylethyl)-1-methyl-6-phenacylpiperidine
lucanthonum lucanthone	1-(2-diethylaminoethylamino)-4-methylthiaxanthone
macrogolum 400 macrogol 400	polyethylene glycol 400
macrogolum 1000 macrogol 1000	polyethylene glycol 1000
macrogolum 4000 macrogol 4000	polyethylene glycol 4000
macrogoli lauras 600 macrogol laurate 600	mono ester of lauric acid and polyethylene glycol 600
macrogoli oleas 600 macrogol oleate 600	mono ester of oleic acid and polyethylene glycol 600
macrogoli stearas 600 macrogol stearate 600	mono ester of stearic acid and polyethylene glycol 600
macrogoli stearas 1000 macrogol stearate 1000	mono ester of stearic acid and polyethylene glycol 1000
meclozinum meclozine	1-(4-chlorobenzhydryl)-4-(3-methylbenzyl)-piperazine
melarsoprolum melarsoprol	2-[4-(4,6-diamino-2-*s*-triazinylamino)-phenyl]-4-hydroxymethyl-1,3,2-dithiaarsenolidine
mepacrinum mepacrine	3-chloro-9-(4′-diethylamino-1′-methylbutylamino)-7-methoxy-acridine
meprylcainum meprylcaine	2-methyl-2-propylamino-propyl benzoate
mercumatilinum natricum mercumatilin sodium	sodium 8-(2′-methoxy-3′-hydroxymercuripropyl)-coumarin-3-carboxylate (sodium mercumallylate) and theophylline
mersalylum mersalyl	sodium salt of 2-[(3-hydroxymercuri-2-methoxy-propyl)-carbamoyl]-phenoxyacetic acid
methioninum methionine	(±) 2-amino-4-methylthio-butyric acid
methoxaminum methoxamine	2-amino-1-(2,5-dimethoxyphenyl)-propanol-1
methylcellulosum methylcellulose	cellulose methyl ether containing about 30 per cent. w/w of methoxyl
methylpentynolum methylpentynol	3-methylpentyn-1-ol-3

* This name is to replace "levorphanum" ("levorphan"), which had been proposed for the same substance (see *Chron. Wld Hlth Org.*, 7, 311).

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
methyltestosteronum methyltestosterone	17β-hydroxy-17α-methyl-3-oxoandrostene-4
natrii acetrizoas sodium acetrizoate	sodium 3-acetamido-2,4,6-triiodobenzoate
natrii amidotrizoas sodium amidotrizoate	sodium 3,5-diacetamido-2,4,6-triiodobenzoate
neoarsphenaminum neoarsphenamine	sodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-*N*-methylene-sulfoxylate
neostigmini bromidum neostigmine bromide	dimethylcarbamic ester of 3-hydroxy-phenyltrimethylammonium bromide
nicethamidum nikethamide	pyridine-3-carboxylic acid diethylamide
nicotinamidum nicotinamide	pyridine-3-carboxylic acid amide
nortestosteroni cypionas nortestosterone cypionate	17β-(3-*cyclo*pentylpropionoxy)-3-oxoestrene-4
oestradioli benzoas oestradiol benzoate	3-benzoyloxy-17β-hydroxyoestratriene-1,3,5 (10)
oestradiolum oestradiol	3,17β-dihydroxyoestratriene-1,3,5 (10)
oestronum oestrone	3-hydroxy-17-oxoestratriene-1,3,5 (10)
pamaquinum pamaquin	8-(4-diethylamino-1-methylbutylamino)-6-methoxyquinoline salt of 2,2′-dihydroxy-1,1′-dinaphthylmethane-3,3′-dicarboxylic acid
pentaquinum pentaquin	8-(5-*iso*propylamino-pentylamino)-6-methoxyquinoline
pentetrazolum pentetrazol	pentamethylene-1,5-tetrazole
pentolonium pentolonium	1,5-(1,1′-dimethyl-2,2′-dipyrrolidyl)-pentane
pethidinum pethidine	ethyl 1-methyl-4-phenyl-piperidyl-4-carboxylate
phenacainum phenacaine	N^1,N^2-bis-(4-ethoxyphenyl)-acetamidine
phenacetinum phenacetin	acetyl-4-phenetidine
phenazonum phenazone	2,3-dimethyl-1-phenyl-5-pyrazolone
phenazopyridinum phenazopyridine	2,6-diamino-3-phenylazopyridine
phenobarbitalum phenobarbital	5-ethyl-5-phenyl-barbituric acid
phenobarbitalum natricum phenobarbital sodium	sodium salt of 5-ethyl-5-phenyl-barbituric acid
phenylhydrargyri boras phenylmercuric borate	equimolecular compound of phenylmercuric borate and phenylmercuric hydroxide

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
phenytoinum phenytoin	5,5-diphenylhydantoin
pramocainum pramocaine	1-[3-(4-morpholino)-propoxy]-4-butoxybenzene
primidonum primidone	5-ethyl-5-phenyl-4,6-dioxo-hexahydropyrimidine
progesteronum progesterone	3,20-dioxopregnene-4
proguanilum proguanil	N^1-4-chlorophenyl-N^5-*iso*propylbiguanide
propoxycainum propoxycaine	2-diethylaminoethyl 4-amino-2-propoxybenzoate
quinisocainum quinisocaine	1-(2-dimethylaminoethoxy)-3-butyl*iso*quinoline
reserpinum reserpine	alkaloid from the roots of *Rauwolfia serpentina* Benth.
riboflavinum riboflavine	6,7-dimethyl-9-(D-1′-ribityl)*iso*-alloxazine
secobarbitalum secobarbital	5-allyl-5-(1-methylbutyl)-barbituric acid
solasulfonum solasulfone	tetrasodium salt of 4,4′-bis-(3-phenyl-1,3-disulfopropylamino)-diphenylsulfone
sorbimacrogoli oleas 100 sorbimacrogol oleate 100	mono ester of oleic acid and tripolyethyleneglycol 100-sorbitan ether
sorbimacrogoli oleas 300 sorbimacrogol oleate 300	mono ester of oleic acid and tripolyethyleneglycol 300-sorbitan ether
stilbamidini isethionas stilbamidine isethionate	1,2-bis-(4-amidinophenyl)-ethene di-(2-hydroxyethane)-sulfonate
succinylsulfathiazolum succinylsulfathiazole	2-(N^4-3-carboxypropionyl-sulfanilamido)-thiazole
sulfadiazinum sulfadiazine	2-sulfanilamidopyrimidine
sulfadiazinum natricum sulfadiazine sodium	sodium derivative of 2-sulfanilamidopyrimidine
sulfadicramidum sulfadicramide	N^1-(3,3-dimethylacroyl)-sulfanilamide
sulfaguanidinum sulfaguanidine	N^1-amidinosulfanilamide
sulfamerazinum sulfamerazine	2-sulfanilamido-4-methylpyrimidine
sulfamerazinum natricum sulfamerazine sodium	sodium derivative of 2-sulfanilamido-4-methylpyrimidine
sulfanilamidum sulfanilamide	4-aminobenzenesulfonamide
sulfaproxylinum sulfaproxyline	N^1-(4-*iso*propoxybenzoyl)-sulfanilamide

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
sulfarsphenaminum sulfarsphenamine	disodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-*N*,*N*′-bis-methylenebisulfite
sulfathiazolum sulfathiazole	2-sulfanilamidothiazole
suspensio insulini cum zinco (amorphum) insulin zinc suspension (amorphous)	a sterile buffered suspension of the amorphous form of insulin with zinc chloride
suspensio insulini cum zinco (crystallisatum) insulin zinc suspension (crystalline)	a sterile buffered suspension of the crystalline form of insulin with zinc chloride
testosteronum testosterone	17β-hydroxy-3-oxoandrostene
tetrabarbitalum tetrabarbital	5-ethyl-5-(1-ethylbutyl)-barbituric acid
tetracainum tetracaine	2-dimethylaminoethyl 4-butylaminobenzoate
tetracyclinum tetracycline	1-dimethylamino-1,4,6,11,12,13,14,18-octahydro-2,5,7,11,14-pentahydroxy-4,6-dioxo-11-methylnaphthacene-3-carbonamide
thialbarbitalum thialbarbital	5-allyl-5-(2-*cyclo*hexenyl)-2-thiobarbituric acid
thiaminum thiamine	3-(4-amino-2-methyl-5-pyrimidinylmethyl)-4-methyl-5-(2-hydroxyethyl)-thiazolium chloride
thiopentalum natricum thiopental sodium	mono-sodium salt of 5-ethyl-5-(1-methylbutyl)-2-thiobarbituric acid
thiotetrabarbitalum thiotetrabarbital	5-ethyl-5-(1-ethylbutyl)-2-thiobarbituric acid
tolonii chloridum tolonium chloride	3-amino-7-dimethylamino-2-methyl-phenazathionium chloride
tosylchloramidum natricum tosylchloramide sodium	sodium toluene-4-sulfonylchloramide
tretaminum tretamine	2,4,6-tri-(ethyleneimino)-*s*-triazine
tricyclamoli chloridum tricyclamol chloride	(±) 1-(3-*cyclo*hexyl-3-hydroxy-3-phenylpropyl)-1-methylpyrrolidinium chloride
tryparsamidum tryparsamide	sodium *N*-phenylglycylamide-4-arsonate
viomycinum viomycin	an antibiotic obtained from certain strains of *Streptomyces puniceus* or *Streptomyces floridae*

Just published

PHARMACOPOEA INTERNATIONALIS

EDITIO PRIMA

Volumen II

INTERNATIONAL PHARMACOPOEIA

FIRST EDITION

Volume II

xx + 350 pages, clothbound
217 monographs
26 appendices

Price: **£1 15**s. **$5.00** Sw.fr **20.—**